between the cysteine residues of the] C-terminal of the β chain [is greater or lesser that 14] is contained between amino acids 193 and 252.

REMARKS

The Office Action mailed March 21, 2000, has been received and its contents carefully noted. Applicant(s) acknowledge with thanks the Examiner's decision to allow claims 1, 3-8, 10, 12, 14, 15, 17, 20, 23, and 26. The Examiner has identified the following issues in the case:

(a) the oath or declaration remains defective;

(b) rejection of claims 2, 9, 11, 13, 22, 24, 25, under 35 U.S.C. § 112 as indefinate for failing to distinctly claim subject matter:

(c) claim 2 and 22 refer to SEQ ID NOs 7, 8, 9, and 10, which are not contained in the application;

(d) claim 9 is indefinite because it is not clear what a CD4 derivative is;

(e) grammatical errors

(f) claim 24 refers to amino acid fragments without identifying SEQ ID Nos;

(g) claim 25 does not further limit claim 1, from which it depends;

(h) rejection under 35 U.S.C. § 112, first paragraph for lack of enablement.

Claims 1-18, 20, and 22-26 are now active in the Application and are believed to be in allowable condition.

The Examiner objected to the oath or declaration.

Applicant submit herewith a new Supplemental Declaration, as Exhibit 1.

The rejection of claims 2, 9, 11, 133, 22, 24, and 25 under 35 U.S.C. §112, second paragraph, has been obviated by the amendments made herein to the claims.

Claims 2 and 22 were rejected for failure to supply Sequence Listings for SEQ ID NO s 7, 8, 9, and 10. The sequence listing is supplied herewith.

Claim 9 is rejected as indefinite on the grounds that it is not clear what a CD4 derivative includes or excludes. Applicants submit that the term "derivatives" is a synonym of "derived molecule", which is defined page 7, lines 19-21 of the specification, where it is recited that "a derivative molecule retains the ligand property of the whole molecule". That means for skilled person that all the molecules having this functional property is included in this term "derivative".

With respect to a specific term, applicants submit that it is well know in the case law that the terms recited in claims should not be read in a vacuum. The Federal Circuit has considered this issue in many instances. For example, in *Morton International Inc, v. Cardinal Chemical Co.,* 5 F.2d 1464, 28 USPQ2d 1190, 1994 (Fed. Cir. 1993), on *remand from,* 113 S.Ct. 1967, 26 USPQ2d 1721 (1993) the court stated the following:

> Whether the claim is invalid for indefiniteness requires a determination whether those skilled in the art would understand what I claimed when **the claim is read in light of the specification reasonable apprise those skilled in the art of the scope of the invention, § 112 demands no more...**(emphasis added);

It is clear from the teachings of the specification, for example at least on page 7, that the term "derivatives" is clearly defined such that a skilled artisan would know what the scope of the claimed invention would be.

Thus, it would be clear to the skilled artisan, applying the common general knowledge in this particular art and the description in the specification what the terminology "Derivatives" encompasses in the claims.

Claims 11, 13, 18, 24, and 25 have been corrected as the Examiner suggested.

In Claim 11 "contains" has been chanced to "containing" as suggested.

In claim 13 "transduced" has been changed to "transducing" as suggested.

In claim 18, "medicament" has been changed to "pharmaceutical preparation" as suggested.

SEQ ID NO's have been supplied for claim 24.

Claim 25 has been re-written in a manner that limits claim 1, from which it depends,

The rejection of claims 9 and 18 under 35 U.S.C. §112, first paragraph, have been obviated by the amendments made herein to claims and in view of the arguments which follow.

(a) The Examiner has rejected claims based on the unpredictability of the results with regards to immunotherapy.

Applicants submit as Exhibit 2, an article by Shinya, *et al.* wherein a soluble multimeric C4BP α chain -CD4, s multi CD4, is used *in vitro* and *in vivo.* This publication demonstrates the following:

- i. *in vivo* expressed anti-viral CD4 is shown in figure 2, pages 476 and 477, under chapter "plasma s Multi CD4 retains its capacity to inhibit HIV infection";

- ii. the plasma level of s Multi CD4 is higher than the plasma level of s Mono-CD4 (see page 479, bottom of the second column and figure 3).

(b) The Examiner objected that "Further, the instant application claims fusion proteins, e.g. containing antibodies, for treating various diseases but has not disclosed any specific constructs that may be effective in such treatments."

Applicants respectfully draw the Examiner's attention on the article of Christiansen *et al.* (Exhibit 3). In this paper, the authors show that, *in vivo*, an octameric sCD46 - C_4bp α fully protects CD46 transgenic mice against a lethal intracranial measle virus challenge. See page 4676, last paragraph, before Discussion.

(c) The Examiner has rejected claims based on the unpredictability of the efficacy of heteromultimers.

Applicants draw the Examiners attention to the publication by Oudin *et al.*(Exhibit 4), which describes the design of an heterofunctional molecule based on the C-terminal part of the α-chain of C_4bp either with CR1 or ScFv anti-D.

This publication shows that:

- i the C-terminal part of the α chain of C_4bp is efficient to induce polymerization during protein synthesis and that although the expression vector codes only for a monomer, multimers are assembled in the cells without any secondary modifications, resulting in the secretion of a unique covalently linked soluble molecule;

- ii a 167 base-pairs corresponding to the C-terminal α fragment of $C_{4}bp$ is enough to obtain this polymerization;

- iii the obtained multimerizing molecule is capable to retain the functional properties of both CR1 and ScFv anti Rh (D) = they are able to bind erythrocytes and to restore or enhance the immune complexes capture by erythrocytes.

Thus, as far as all primates, including humans, use erythrocytes bearing CR1 to eliminate immune complexes, these results, taken together with *in vivo* results of Exhibit 1, show that the *in vivo* effect obtained with mice should *a forciori* been observed in primates and these heteromultimers usable as substitutive or epurative therapy in human plasma.

Applicants submit that the disclosure in the specification, completed by the disclosure of Exhibits 2, 3, and 4 teach:

i. - how to make and purify fusion protein and derivatives (with above the comments about derivatives);

ii. - that such heteromultimerized molecules are efficient *in vitro* and *in vivo*, and

iii. that the comments of Rindinger *et al.* cannot applied in this case since derivatives are defined as molecules retaining the biological property of the parent molecule.

In view of the foregoing amendments and remarks, it is requested that the rejections of record be reconsidered and withdrawn, that claims 2, 11, 13, 18, 22, 24, and 25 as amended be

allowed, in addition to allowed claims 1, 3-8, 10, 12, 14, 15, 17, 20, 23, and 26, and that the Application be found to be in allowable condition.

Should the Examiner not find the Application to be in allowable condition or believe that a conference would be of value in expediting the prosecution of the Application, Applicants request that the Examiner telephone undersigned Counsel to discuss the case and afford Applicants an opportunity to submit any Supplemental Amendment that might advance prosecution and place the Application in allowable condition.

Respectfully submitted,

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Enclosures(4)